REMARKS

The present response is intended to be fully responsive to all points of objection and/or rejection raised by the Examiner and is believed to place the application in condition for allowance. Favorable reconsideration and allowance of the application is respectfully requested.

Applicants assert that the present invention is new, non-obvious and useful. Prompt consideration and allowance of the claims is respectfully requested.

Status of Claims

Claims 1-27 are pending in the application. Claims 1-27 have been rejected. Claims 1, 6-7, 11-12, 18-19, 23 and 25-26 have been amended.

Claims 2-4, 8, 12-16, 20-22 and 27 have been canceled without prejudice or disclaimer. In making this cancellation without prejudice, Applicants reserve all rights in these claims to file divisional and/or continuation patent applications if applicable.

New claims 28-29 have been added in order to further define what the Applicants consider to be the invention. Applicants respectfully assert that no new matter has been added.

Applicants respectfully assert that the amendments to the claims add no new matter.

Double Patenting Rejections

In the Office Action, the Examiner rejected claims 1-27 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of U.S Patent Serial No. 6,692,766.

Applicants hereby offer to provide a terminal disclaimer upon indication by the Examiner of allowable claims.

CLAIM REJECTIONS

35 U.S.C. § 103 Rejections

In the Office Action, the Examiner rejected claims 1-27 under 35 U.S.C. § 103(a), as being unpatentable over Akiyama et. al., in view of German Patent document DD252,539 (the '539 Patent) and Bar Shalom et al..

Applicants respectfully traverse the rejection of claims Akyama et al., under the '539 Patent and Bar Shalom et al..

According to the Examiner, Akiyama et al. teaches a matrix comprising a viscogenic agent, namely an acrylic acid polymer, a polyglycerol fatty acid ester (abstract), peptide active agents are specified (col. 8, lines 11-24), alternative viscogenic agents including carboxymethyl cellulose and algin are disclosed (col. 3, lines 14-23, col. 3, line 58 – col. 4), enteric coating is specified (Col. 11, line 46 – col. 12, line 7) and tablets are disclosed (col. 13, lines 41-42). The Examiner further noted that Akiyama et al. disclose hydrophobic polyglycerol fatty acid esters (col. 5, lines 13-17) and that starch is also disclosed (col. 10, line 8).

Further according to the Examiner, '539 teaches the addition of an absorption promoter and a protease inhibitor to assist in absorption and prevent deactivation respectively of a proteinaceous drug.

The Examiner asserts that it would have been obvious to one of ordinary skill to add an absorption promoter and a protease inhibitor to the composition of Akiyama et al. to achieve the beneficial effect of assisting absorption and prevent degradation respectively of a proteinaceous drug in view of '539.

Applicants respectfully traverse.

The present invention relates to a drug delivery composition which is characterized by specific structure and specific function, namely:

Structure: an erodable hydrogel-forming polymeric matrix which comprises (1) a blend which comprises (i) a hydrophilic polymeric cellulose derivative and (ii) a hydrophobic polymeric acrylic acid derivative; (2) a drug; (3) an agent which

enhances intestinal drug absorption; and (4) an agent which inhibits intestinal drug degradation.

Function: wherein erosion of said erodible matrix permits synchronous release of said drug, said agent which enhances intestinal drug absorption and said agent which inhibits intestinal drug degradation.

The composition disclosed by Akiyama is different in both structure and function, as follow:

Structure: a matrix particle having a melting point of 30° to 120°C, which comprises (1) a specified polyglycerol fatty acid ester; (2) a drug; and (3) an agent which becomes viscous on contact with water selected from acrylic acid polymers and their salts.

Function: gastrointestinal mucosa-adherent. (cf. claim 1 of Akiyama)

Component (1) of Akiyama is hydrophobic. This is the major component of the matrix particle, as can be realized from the Examples. Thus, in Example 2 components (1) and (3) are used at a weight ratio of 10:2 (about 83% of (1)), and this ratio decreases in the other Examples,, e.g. a ratio of 11.5:0.5 (about 96% of (1)) in Example 2, 17:1 (about 94% of (1)) in Example 6 and so forth. Component (3), which becomes viscous upon contact with water, is used to increase the muco-adhesive properties of the matrix particle, and is used in very minor quantities, and thus the matrix particle of Akiyama is essentially hydrophobic.

In contrast to Akiyama, that teaches a mixture of a viscogenic agent, namely an acrylic acid polymer and a polyglycerol fatty acid ester The present invention relates to the use of a specifically defined hydrophobic polymer, namely polymethacrylate (such as Eudragit RL and RS), which are also known as ammonio-metharylate copolymers. The polymethacrylate is used in combination with hydrophilic cellulose derivatives. It should be stressed that polymethacrylate is very different from polycarbophil or Carbopol mentioned in Akiyama's patent. Polycarbophil and Carbopol are well known hydrophilic acrylic (and not methacrylic) acid polymers crosslinked with divinyl glycol, and they can be used as viscogenic agents. Polymethacrylates, as claimed in present claim 1, are not viscogenic and they cannot be

replaced by alternatives such as carboxymethyl cellulose and algin, referred to by the Examiner.

In the composition of the invention, the matrix is essentially hydrophilic (hydrogel-forming) and is not viscous (cf. Examples, page 18, Preparation of Polymer, line 5: "*low-viscous gels were formed*"). The major component is the hydrophilic component (i), and the hydrophobic component (ii) is added for achieving erodability in aqueous environment. This hydrophobic component does not become viscous upon contact with water.

Referring to function, the approach in the present application is completely different, i.e. a hydrogel matrix which travels, while eroding and synchronously releasing the active agents, along the whole of the GI tract. The rate of release of the active agents is determined by the rate of erosion of the hydrogel, and thus all active agents are synchronously released.

In contrast, in Akiyama the particle is to be retained in a specific locus of the GI tract, by adhering to the mucosa, i.e. the particle is essentially static. This can be well seen from Table 1 of Akiyama, which shows that even 8 hours post administration, 47.4% of the particle could tracked. The system of Akiyama is not erodable, and the active agent is released by diffusion, the rate of which depends on its molecular weight. Thus, agents with different molecular weight would be released at completely different rate. Importantly, for peptide drugs with high molecular weights, the rate of release would be minimal, and it is not surprising the Akiyama exemplifies release of small molecules.

Turning now to the '539 document, the Examiner alleges that it would have been obvious to the man of ordinary skill to add the degradation inhibitor and absorption enhancer of '539 to the particle of Akiyama, to obtain the composition of the invention.

This is clearly not the case. First of all, considering the different functional mechanisms (viscous muco-adherent essentially static hydrophobic particle which releases the active agent by diffusion vis-a-vis a low-viscosity erodable hydrogel which releases the active agents at

rate of its own erosion), there would have been no motivation for the man of skill in the art to combine the teachings of Akiyama and '539.

Moreover, as explained above, even if one tried to add the degradation inhibitor and absorption enhancer of '539 to the particle of Akiyama, a synchronous release of the drug and the other agents would not be achieved, since these three agents, grossly differing in their molecular weights, would be released at different diffusion rates, and not synchronously, as achieved by the erosion property of the composition of the invention.

Therefore, it is respectfully submitted that the invention is not obvious over Akiyama in view of '539.

With regards to Bar Shalom et al., in response, Applicants cancelled the claim to multi-layered tablets thus making the rejection moot.

An obviousness rejection requires a teaching or a suggestion by the relied upon prior art of all the elements of a claim (M.P.E.P. §2142). Since as amended, the Examiner fails to establish a prima facie showing that Akyiama et al., or the '539 Patent, or Bar Shalom et al., alone or in combination, teach or suggest every feature of claim 1.

Applicants note that none of the amendments to the claims herein are in response to the above discussed prior art rejections.

In view of the foregoing amendments and remarks, the pending claims are deemed to be allowable. Their favorable reconsideration and allowance is respectfully requested.

Should the Examiner have any question or comment as to the form, content or entry of this Amendment, the Examiner is requested to contact the undersigned at the telephone number below. Similarly, if there are any further issues yet to be resolved to advance the prosecution of this application to issue, the Examiner is requested to telephone the undersigned counsel.

Please charge any fees associated with this paper to deposit account No. 50-3355.

Respectfully submitted,

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